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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/776,874	02/06/2001	Iris Pecker	01/21603	8407

7590 07/01/2004

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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/776,874	PECKER ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *64-67 and 70-79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *64-67 and 70-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/19/2004 has been entered.

Applicants cancellation of claims 14-63, 68 and 69 and amendment of claims 64, 66 and 70 and the addition of claims 71-79, in the Paper of 4/19/2004, is acknowledged.

Claims 64-67, 70-79 are still at issue and are present for examination.

Applicants' arguments filed on 4/19/2004 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Specification

The disclosure is objected to because of the following informalities:

Applicants previous amendment, 10/1/2003, of the specification at page 54, lines 14-16 to recite "Insect cells are known to produce proteins free of PAI1 (type1

plasminogen activator inhibitor)." is objected to because this recitation is not supported by the original specification and is therefore considered new matter.

Applicants did not respond to this objection in the response of 4/19/2003.

Appropriate correction is required.

Claim Objections

Claims 76-78 are objected to because of the following informalities:

Claims 76-78 are duplicates of claims 73-75, respectively.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 64-67 and 70-79 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a protein or preparation comprising said protein having the amino acid sequence of SEQ ID NO: 10, said protein having heparanase activity or being so cleavable so as to acquire said heparanase activity, does not reasonably provide enablement for any protein or preparation comprising said protein having heparanase activity or being so cleavable so as to acquire said heparanase activity, wherein said protein is merely 90% homologous to SEQ ID NO: 10 or a portion thereof, said protein being capable of eliciting an anti-heparanase antibody.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was made in the previous office action. In response to this rejection applicants have amended claims 64, 66 and 70 and added new claims 71-79 and traverse the rejection as it applies to the new claims.

Applicants traverse this rejection as it applies to claims 64-67, 70, 71-79, on the basis that as described in the Declaration of Iris Pecker submitted in U.S. Application 09/988,113 and attached as Appendix 1, heparanase from mouse has a homology of about 80% and that of chick has less then 70% homology to human heparanase, yet these proteins are still clearly recognizably heparanase, as they retain heparanase functionality and have a similar level of activity. Thus applicants submit that those heparanase proteins having a sequence of at least 90% homology to human heparanase are well within the level of homology that could be expected for heparanase. While applicants argument is acknowledged, and is appreciated, just because it could be appreciated that their exist proteins having at mere 90% homology to human heparanase, while retaining heparanase activity, applicants have not presented guidance as to how to determine and make a majority of those molecules of the claimed genus.

Further, while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants (i.e., having heparanse activity) requires

that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish those characteristics which are necessary to enable such a broad genus as previously stated (i.e. (A) regions of the protein structure which may be modified without effecting heparanase catalytic activity; (B) the general tolerance of heparanases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a heparanase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful).

Applicants further submission, that applicant has submitted alignment data showing the homology between human, rat, mouse and chicken heparanase sequences as well as important shared features such as the heparan sulfate binding site is acknowledged. While this information is helpful in enabling the claimed genus, by itself it appears to be insufficient to do such.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to **make** and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any heparanase having a mere 90% homology to SEQ ID NO: 10. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 64-67 and 70-79 are rejected under 35 U.S.C. 102(b) as being anticipated by Fuks et al. (U.S. Patent No. 5,362,641).

The rejection was originally stated in the previous office actions, 10/21/2003, 7/1/2003 and 12/17/2003. In response to this rejection applicants have amended claims 64, 66 and 70 and added new claims 71-79 and traverse the rejection as it applies to the new claims. Newly added claims 71-79 are included in the rejection for the same reasons previously stated for claims 64, 65, 66, 67, 69 and 70. Further it is noted that the protein taught by Fuks et al. anticipates claims 73-79 even though Fuks et al. may

not specifically teach production of the protein recombinantly. While the reference does not specifically disclose the enzyme produced by recombinant production (as recited by the claims), the production of a protein by a particular process does not impart novelty or unobviousness to a protein when the same protein is taught by the prior art. This is particularly true when the properties of the protein are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicants continue to traverse this rejection along many of the lines of argument presented in the previous office action. Applicants argue that for a rejection to be made under 35 USC 102, all of the limitations of the claim must be explicitly taught by the reference, and Fuks et al. does not teach or suggest the particular sequences of any protein. As previously stated, applicants are reminded that the heparanase taught by Fuks et al. **inherently** has an amino acid sequence which meets the limitations of the rejected claims, and thus Fuks et al. need not teach this specific sequence in order to anticipate the claims.

Much of applicants argument is on the basis that Fuks et al. does not render any of these claims obvious, because as previously described in the previously filed Response and Declaration, actually determining the sequence of heparanase for the first time proved to be a non-trivial task. Applicants entire argument based on the above is acknowledged, however, found nonpersuasive because applicants continues to be reminded that this is a rejection based on anticipation, not obviousness and the protein taught by Fuks et al. anticipates the rejected claims.

Applicants argument that Fuks et al. does not teach the sequence of the purified heparanase is not found persuasive as a teaching of the sequence of the taught heparanase is unnecessary as the taught heparanase inherently has the claimed sequence.

Applicants argument that Fuks et al. failed to obtain pure heparanase is not found persuasive because applicants current claims have no purity limitation that would not be anticipated by Fuks et al.

Applicants argument that if the person skilled in the art chose to perform the taught purification process of Fuks et al. through the final suggested purification step, such a person would be confronted with a mixture of proteins, is acknowledged, however not found persuasive as applicants currently rejected claims only necessitates "An isolated protein having heparanase catalytic activity..." and does not preclude the presence of potentially additional contaminating proteins.

Thus applicants argument has been considered in full and found to be non-persuasive.

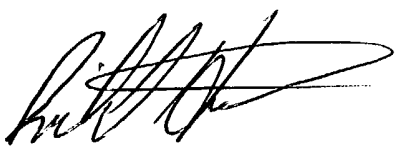
Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

Rgh
6/22/2004